DETERMINING OPTIMAL MEDIAL-LATERAL RESECTION ANGLE FOR VARUS PATIENTS UNDERGOING A TOTAL KNEE ARTHROPLASTY

by

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I have read the thesis of Megan Elizabeth Aanstoos in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the supervisory committee and is ready for submission to The Graduate School.

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ABSTRACT

Soft tissue and ligament imbalancing has been documented as a contributor to excessive wear in total knee arthroplasty (TKA). Conventional surgical techniques realign the varus proximal tibia to a neutral angle with the anatomical axis of the tibia during TKA. This modification can require additional operative procedures, including rebalancing of the ligaments and intraoperative alignment. David Scott, our collaborative surgeon, stated that he has "little to no need" to re-balance the ligaments when resecting a varus patient to 2° of varus during a primary TKA. Although an apparent clinical advantage, little was known as to how this resection technique might affect the properties of the cancellous bone, which are important since failure of bone can lead to instability and failure of the implant fixation.

A collaborative study was conducted with Institutional Review Board (IRB) approval. The general hypothesis tested that resecting the proximal tibia of a varus patient at a 2° varus angle would not affect bone strength or trabecular orientation compared to a neutral resection angle. The study tested the compressive strength of cancellous bone as well as examined trabecular orientation/degree of anisotropy of the cancellous bone to determine if there were differences.

Mechanical testing used a penetration method to measure compressive strength. Bone specimens were cut from the proximal tibia of the patient and sent from WA to UT

for mechanical testing. MicroCT images of each specimen were also obtained in order to visualize trabecular alignment.

The data confirmed no difference in the compressive strength between the neutral and varus ($p=0.87$ and $p=0.71$) resection techniques. Additionally, no difference was found amongst three tibia regions ($p=0.16$, 0.16, 0.34, 0.73, 0.62). Finally, degree of anisotropy values for the cancellous bone were not different between the two resection angles ($p=1.00$).

The data collected during this study demonstrated that cutting the proximal tibia at a 2° varus angle during a primary TKA of a varus patient does not compromise the compressive strength of the proximal tibia. Furthermore, using the varus cut may reduce the need for ligament balancing, as noted by our collaborative surgeon, while reducing surgical time without compromising implant fixation.

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ACRONYMS AND DEFINITIONS

Anatomical Axis .... AA

Anterior Cruciate Ligament .... ACL

Degree of Anisotropy .... DA

Institutional Review Board .... IRB

Lateral Collateral Ligament LCL

Mean Intercept Length .... MIL

Mechanical Axis .... MA

Medial Collateral Ligament .... MCL

Microcomputed Tomography .... MicroCT

Osteoarthritis .... OA

Posterior Cruciate Ligament .... PCL

Range of Motion .... ROM

Rheumatoid Arthritis .... RA

Scanning Electron Microscope .... SEM

Total Knee Arthroplasty .... TKA

Anisotropy (degree of): A measure of organization of the structure. The organization of the material decreases with a higher degree of anisotropy.

Eigenvalues: Scalar value giving the magnitude of the eigenvector. In this study, a larger eigenvalue signifies a higher correlation between the trabecular orientation and the corresponding eigenvector. The principle eigenvalue is in the same direction as the majority of the trabeculae.

Eigenvectors: Vectors signifying the direction, in this study, of the trabeculae.

Neutral: Perpendicular to the anatomical axis of the tibia when the axes are drawn on a long-standing x-ray.

Trabecular orientation: Direction of the trabeculae of cancellous bone.

Valgus: Deformity of the, in this study, proximal tibia which results in an angle such that the patient's leg deviates outward.

Varus: Deformity of the, in relation to this study, proximal tibia which results in an angle such that the patient's leg deviates inward.

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INTRODUCTION

Total Knee Arthroplasty

Nearly 400,000 primary total knee arthroplasty (TKA) surgeries are performed each year in the United States[1] at a cost of $20,000 to $35,000 per procedure.[2] Additionally, there are over 30,000 revision TKA surgeries done each year, which cost the healthcare industry over $870 million annually.[3] Reducing the total number of TKA revisions by just 1% would translate into an annual savings of over $8.7 million.

TKA failure modes that result in revision surgeries include component loosening, instability, sepsis, extensor mechanism power loss, poor range of motion (ROM), bone fractures and prosthesis fracture.[4] Other causes of failure include malposition and failure of fixation.[5] Because failures not only cost money, but also include a physical and emotional toll with each additional surgery, it is important to find ways to minimize revision surgery.

In a study of 279 patients, Fehring et al. documented that 13% of the implants failed due to instability. Furthermore, if all the patients had correctly balanced ligaments and soft tissues, the number of revisions would have decreased by 40% and overall failures would have been reduced by 25%.[6] Dorr and Boiardo affirm that "malaligment is the number one cause of loosening," and reiterate that incorrect rotation or placement can cause side-to-side movement.[7] If this happens on the tibial tray, it can cause excessive wear damage and exacerbate the failure process.[8] Instability can be corrected by appropriately balancing the knee ligaments during the primary surgery. Because the proximal tibia has been shown as a common site of component mechanical failure, finding a way to optimize mechanical strength of the bone and keep the ligaments balanced is an integral part of reducing the revision rates of TKA surgeries in the United States.[9, 10]

Knee Alignment

Two axes of importance to the tibia must be considered during TKA. The first of these is the anatomical (tibial shaft) axis, and the second is the mechanical (functional) axis. The anatomical axis is a line that connects the center of the intramedullary canal at the proximal third and distal third of the tibia[11] and also characterized by the angle formed by the axis of the femoral and tibial bones.[7] A line that connects the center of the tibial plateau and center of the talar dome defines the mechanical axis[11] and, when considering the entire lower extremity as one unit, it can also be determined by a line joining the center of the femoral head to the center of the knee joint to the center of the ankle joint (Figure 1).[7]

For neutral knee patients, the two axes are not in conflict with each other and are the same. In this case, the femur would be perpendicular to the mechanical axis of the femur and the tibial component would be perpendicular to the tibial shaft. However, in varus knee deformity, the mechanical axis changes location and therefore the axes used for neutral alignment may no longer be applicable. A higher severity of varus creates a larger difference between the axes.[11] Matsuda et al. recommend that surgeons select the axis with the best postoperative alignment, minimal bone loss, and optimal ROM for the patient.[11] Because every knee is unique, each patient's physiology at time of TKA must

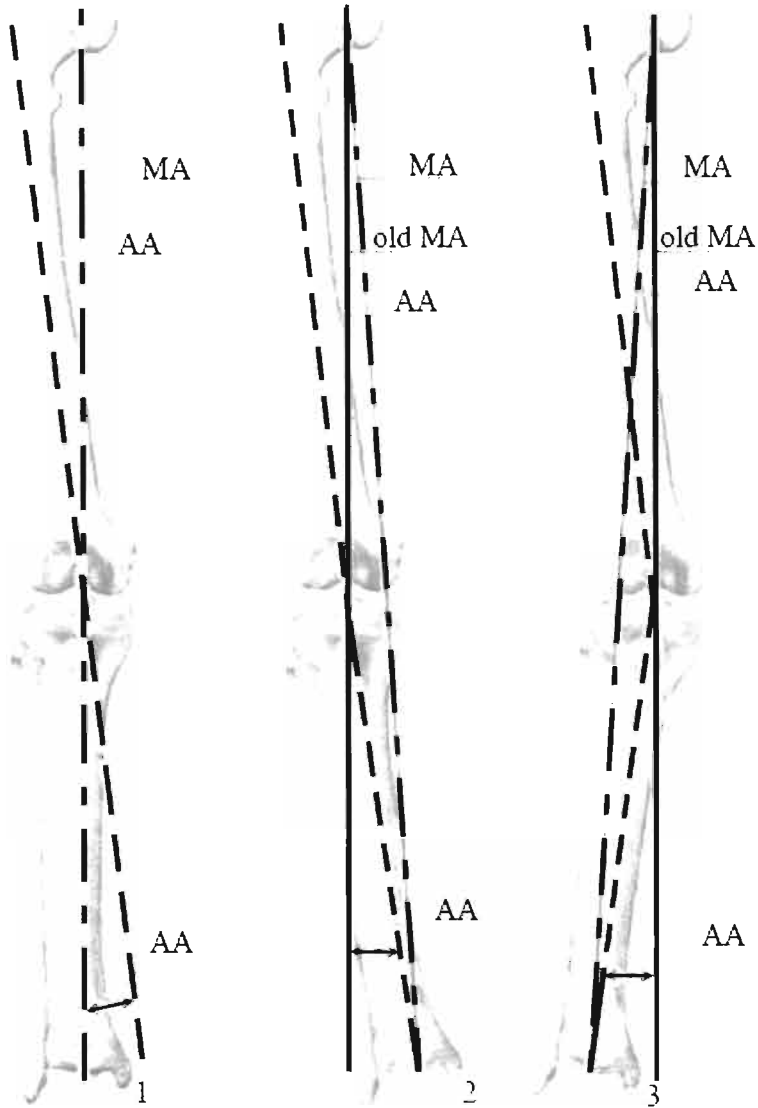

Figure 1. Pictorial representation of knee axes. Image 1 depicts a neutral knee with the anatomical axis (AA) and mechanical axis (MA). Image 2 represents a varus knee and image 3 a valgus knee with AA and MA axes shifted for both. To compare, the MA for the neutral knee (old MA) is shown as well in images 2 and 3. The top AA uses a definition from Matsuda et al., and the bottom AA refers to the definition given by Dorr et al..[7, 11] This set of images demonstrates the importance of choosing one axis during surgery and matching the natural physiology of the patient. Figure adapted from Marti et al.[12]

be taken into account when planning surgical procedures and choosing implants. The axis chosen by the surgeon should maintain appropriate anatomical alignment without threatening the mechanical stability of the implant (Figure 1).

Following TKA, the surgeon must be sure to keep the patient in proper anatomical alignment, which translates to varus or valgus tilt to the knee along with flexion-extension [13] and internal-external rotation.[14] Varus or valgus tilt of the knee joint can occur in two cases. The first occurs with a tilted femur with respect to the tibia, creating an angle either at a medial or lateral direction from the tibiofemoral anatomical axis. The second case arises when the tibia has grown tilted, so it does not perfectly align with the femur (Figure 1). An excessive varus tilt of the knee results in a "bow-legged" effect, and a valgus tilt results in a "knock-kneed" condition. A varus angled tilt of the tibia is more common than a valgus angle.[15] These angles can be measured against the neutral tibiofemoral anatomic axis using a goniometer on long standing x-rays.

Mechanical Stability

Although important to consider anatomical alignment, it could also be helpful to optimize mechanical stability of the implant. Tibia component failure for mechanical reasons predominates in TKA, and thus researching this area could help improve stability.[9], [16] Improving engineering design and surgical resection could increase implant stability.

First, engineers had to optimize materials and implant design. This was done by experimenting with different polymers,[17] choosing a metal that exhibits biologically compatible, and selecting an ideal design for the implant shapes. Currently, surgical techniques are becoming increasingly important for optimizing implant longevity. Proper realignment, a crucial component of the operation, can be done by balancing ligaments and soft tissue to optimize mechanical stability. If precise realignment that does not compromise mechanical properties of bone could be achieved, then the wear and revision rate could be reduced, resulting in savings of millions of dollars for the patients and healthcare industry.

One of the first materials used for the tibial tray in TKA was ultra high molecular weight polyethylene. However, the polyethylene wears and creates debris that can lead to osteolysis and implant loosening, which has resulted in a need for revision surgery.[17] In one study conducted by Windsor et al., 1430 cemented primary TKA patients were analyzed. The prostheses were divided into three groups: two groups were comprised of all polyethylene tibial components, and the third had a metal-backed tibial component with interchangeable polyethylene articulating surfaces. It was found that none of the metal-backed tibial components were revised for loosening, while seven of the all polyethylene components failed.[18] These results indicated that metal backed tibial trays may have superior performance.

The advantage of metal backed tibial trays comes from the properties of the metal compared to the polymer as well as the design of the tray. A polymer has more ductility than a metal and deflects differently in response to loads. Because of this, the metal better distributes the loads uniformly across the entire tibial plateau and reduces concentrated loads that impact the weaker regions of bone.[19] Additionally, the modularity of the components allows for better adjustment of the joint line and better distribution of the load. The metal-backed tibial tray, once inserted, can be fitted with several thicknesses of polyethylene until optimal alignment and joint line are reestablished. This use of modular components helped reduce the need for ligament balancing and improved stability of the tibial component.

In addition to prosthetic designs, surgical techniques have also been shown to influence mechanical stability. Townley was the first to advocate in the mid-1980s the idea that the posterior tilt of the tibia is important for good range of motion.[16] This was extensively studied by Hofmann et al. who found that proximal tibia should be resected parallel to the slope of the tibia instead of perpendicular to the anatomical axis along the anterior posterior direction (Figure 2).[20] Mechanical testing of the tibia wafers found that the parallel resection resulted in a mean force of approximately 15 kN while the perpendicular resection had a mean force of 10 kN. Additionally, the parallel resection group had higher stiffness, and in a study of TKA patients, those with a parallel resection had less need for revision due to subsidence.[20] Hofmann et al. also found that the anterior medial region of the tibia was weaker than other regions, which would explain why tibial component subsidence usually occurs in this region clinically.[20]

Bloebaum et al. studied the surface of the tibia in more detail to determine the amount and type of bone present. Their data supported Hofmann et al., and the results provided evidence that the anterior and lateral regions had 31% less bone than posterior-medial regions.[21] This partially resulted from a higher percentage of cortical bone present in the posterior-medial region, which has a higher strength and stiffness than cancellous bone.

Finally, Bachus et al. examined the orientation of trabeculae to determine if trabeculae position corresponded with strength.[22] The outcome of the study revealed

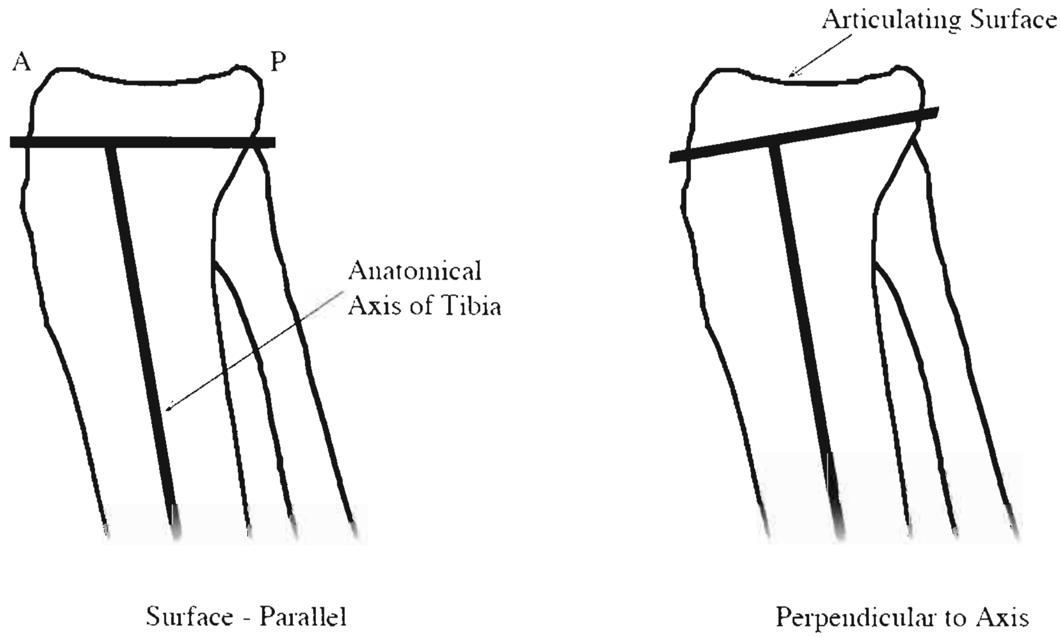

Figure 2. Comparison of anterior-posterior resection angle. Hofmann et al. examined resection technique in an anterior (A) – posterior (P) direction.[20] They determined that the bone was stronger when using the surface-parallel resection technique (left image).

that the trabeculae of the A/P surface parallel technique were oriented nearly vertical compared to perpendicular axis resections. This demonstrated that the trabeculae are less susceptible to bending and helped explain the ability of the cancellous bone to withstand a higher load, as shown by a biomechanical study conducted by Hofmann et al., which used a parallel resection technique.[20] Since resection techniques can influence mechanical stability, they can be an important factor in TKA durability and longevity, and all attempts should be made to optimize material design and surgical technique.

Ligament Balancing

Four primary ligaments surround the knee joint; those being the lateral collateral ligament (LCL), medial collateral ligament (MCL), anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) (Figure 3). During TKA, surgeons generally sacrifice the ACL and the PCL may or may not be scarified. Fehring et al. point out that “total knee arthroplasty is not merely an exercise in bony carpentry” and that care must be given also to the soft tissue and ligaments to avoid early revision due to instability.[6] After a change in the shape of the joint when the prosthetic components are put in place, ligament balancing becomes necessary to restore the joint alignment. [23] Without proper balancing, malalignment can occur and overload the bone, which contributes to

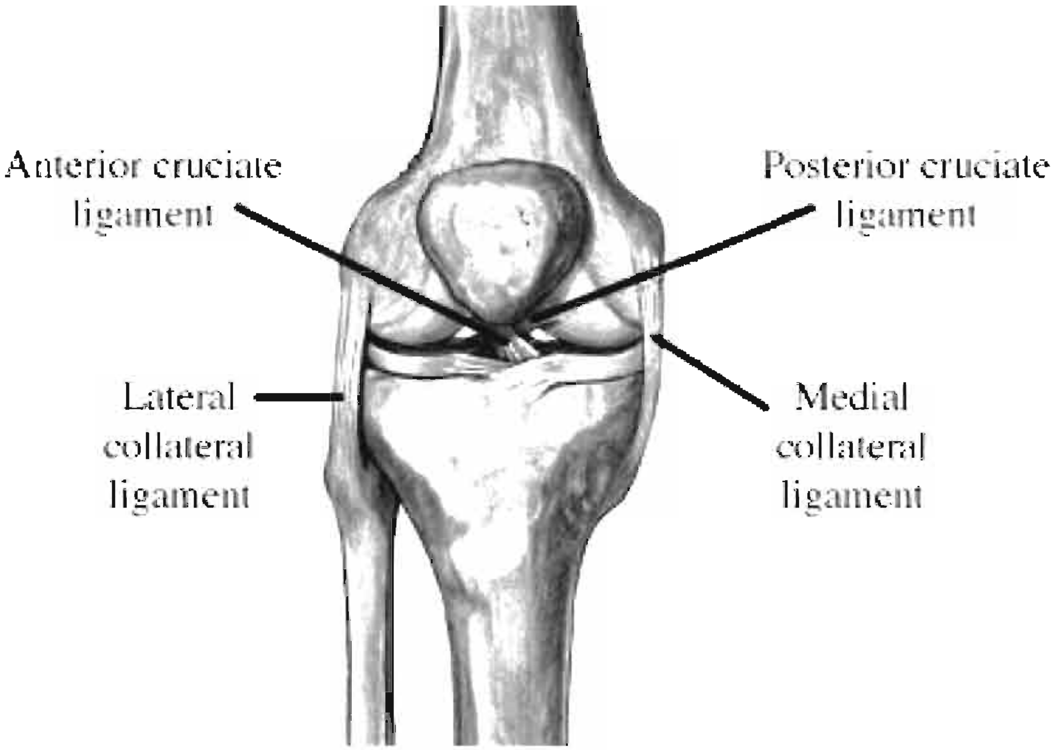

Figure 3. Major ligaments of the knee. Anterior view of a right knee showing all four major ligaments of the knee. Figure adapted from Scholten.[24]

subsidence, instability and prosthetic loosening.[25] Sometimes a surgeon will use a mechanical device to assist in balancing the ligaments[26], [23], [27] but other times the surgeon does so by flexing and extending the knee and correcting position until a normal ROM is achieved.[8], [28, 29]

For a patient with a neutral knee, this process of determining ROM is relatively quick and accurate. However, for patients with a varus or valgus tilt, more operative procedures to correctly balance the ligaments are usually required. In many cases, the balance cannot be completed without a release of the ligaments, which can result in an unstable knee for the patient. More patients have varus deformity than valgus deformity, and it primarily results in issues with the MCL[30], [25] whereby the surgeon must release or otherwise operate on the imbalanced MCL. Krackow points out that, because bone shape varies with a varus deformity, it can change the soft tissue attachments, especially around the femoral epicondyles.[13] Therefore, attempting to "neutralize" the knee could exacerbate the situation instead of resulting in an anatomically neutral knee. Engh, who attempts to "neutralize" the knee, reports that more than 50% of the TKAs done on varus patients at his clinic have resulted in the need for MCL releases.[8] This high number can be contrasted with Dr. Scott's anecdotal report that he does not recall having ever needed to do ligament releasing or balancing on his varus patients. (personal communication) With over 100 TKA surgeries done on varus patients each year (again 50% of his primary TKA patients), Dr. Scott's record can be compared to the number of surgeries reported by Engh.

The differences in surgical technique can therefore have a significant impact on the number of patients that require balancing. Unlike most orthopedic surgeons, Scott uses a 2° varus cutting block when removing the top of the proximal tibia. This keeps his varus patients in varus and, for patients with a varus deformity of 7° or fewer; he does not need to balance ligaments after surgery. Using this technique results in no compromise in flexion, extension, or rotation as occurs when a lateral or medial release technique is utilized. One knee system (The Porous Coated Anatomic Knee System) utilizes a 3° varus tibial resection to reproduce the mechanical axis, which agrees with Hungerford, who feels that, without some varus degree, a tilt will result in stance and gait difficulties.[7] Townley also noted that attempts to "neutralize" the knee to using the anatomical axis usually results in about 2° of varus[16] but this improves with the use of computer assisted technology.

Cancellous Bone Properties

Avoiding ligament balancing benefits the TKA patient; however, the effect on the mechanical properties of the cancellous bone when leaving a patient in varus must be addressed. To resolve this concern, it becomes important to understand the properties of cancellous bone. Both cancellous (trabecular) and cortical (compact) bone types can be found in the tibia. Both bones are made of type I collagen, hydroxyapatite mineral and water. The organization of these materials differentiates the two. The cortical bone has a higher density and lower porosity than cancellous bone (5-30% compared to 30-90%).[31] Bone generally exhibits anisotropic organization although some bones in the body can be categorized into the subclasses of transversly isotropic or orthotropic.[32] Even though both types of bone can be found in the proximal tibia, the focus of this study was on cancellous bone (Figure 4).

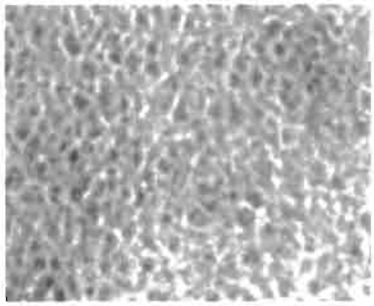

Figure 4. Cancellous bone structure of the human proximal tibia. The image is a radiograph of specimen 011 from the current study.

Singh found that cancellous bone can be classified into three types based upon the structure. Type I was comprised of delicate rods and located in long bones. Type II was a mix of rods and plates and has subtypes based on site and ratio of rods to plates. Usually Type II can be located in long bones, scapula bones, and the calcaneum. Finally, Type III was made up of plates and also has subtypes based on density and orientation. It can be found in the vertebrae, patella and under cartilage in long bones.[33] The rods exhibit lower density properties than the plates. This suggested a relationship between the type and associated mechanical properties with the rods able to handle less mechanical stress than the plates.[34] The biomechanics of cancellous bone are complex and a level of structure must be determined when attempting to characterize the properties. The proximal tibia, where this study was conducted, predominantly has Type II bone.

Keaveny et al. suggest studying the level of bone on the order of 5-10 mm in dimension where the bone behaves as a continuum.[32] On this level, cancellous bone is a composite and anisotropic. The anisotropy of bone changes with age and disease state, which can lead to a more porous structure in the afflicted population. This change partially can be described by Wolff's hypothesis that bone adapts along lines of force.[35] However, other factors can also be significant, as discussed later. When testing cancellous bone for mechanical properties in order to avoid complications from material constraints, which can change based on direction, a principal direction must first be designated.

Determining the composition of the Type II cancellous bone has importance when modeling bone. Carter and Hayes suggested that bone has a two-phase porous structure and that marrow can be negated for strains less than 10.0/s,[31] which means that only the mineral, water, and collagen are relevant for modeling and mechanical testing. In addition, bone quality must be considered during mechanical testing. Bone density and strength determine bone quality but ageing, osteoporosis, osteoarthritis and fracture risk affected the value.[36]

Age decreases compressive strength because it changes the density of the bone, which decreases ability to withstand load. Age can also affect Young's modulus, ultimate stress, and bone volume fraction.[37] Differences in preparation of and testing methods used on the specimen can also modify material property values, and thus complicate comparisons between literature sources.

Osteoporosis, a bone disease, directly affects bone and bone quality. A highly osteoporitic bone requires preoperative decisions due to the poor quality and much weaker structure. Osteoarthritis (OA) and rheumatoid arthritis (RA) are also known to have a secondary affect on cancellous bone near the proximal and distal ends of long bones. The hardness of cancellous bone decreases with both OA and RA, which are degenerative diseases of cartilage.[38] When OA and RA affect the cartilage, which becomes worn, bone exposure occurs. This modification of forces on the bone changes the microstructure of the underlying cancellous bone, which can be seen even in the earlier stages of OA. Ding et al. show that the arthritic change modifies the trabeculae from rod-like to plate-like structures, but it also lowers mechanical properties when compared to normal cancellous bone.[39]

Although this study focused on the proximal tibia, it was imperative to note that cancellous bone properties vary significantly with anatomical location due to bone's heterogenic properties. For the purpose of this study, it was important to refer back to the findings of Bloebaum et al. that the medial region was stronger than the lateral region.[21] The effects of aging and OA on bone can be disregarded if the comparison groups have similar ages and diseases. It can be concluded that cancellous bone properties are complex and not easily classified.

Mechanical Testing

There are several published methods describing how to test compressive mechanical properties of cancellous bone.[40], [41], [31], [42, 43], [44], [10], [45], [46] Most studies of cancellous bone used either cylinders, cubes or a penetration test. Some tests removed marrow and some did not, but according to Carter and Hayes in 1976, only strain rates of 10.0/s and above depend on marrow and anything less did not change the results of a mechanical test.[41] Keaveny et al. used an end-cap method to test cylinders but other studies have used a platens method or a whole wafer method.[42], [20, 47] A totally different approach was taken by Sneppen et al.[46] and Hvid et al.[44] [10], [45] when they developed what they termed an "osteopenetrometer." The machine penetrates cancellous bone and collects forces (in Newtons) from each level of deflection as the needle transverses the cancellous bone. Originally developed as a possible way to test bone quality in the operating room, the schematics of the machine lend themselves well to testing oddly shaped samples of bone.

For this study, the osteopenetrometer method was chosen since the specimen varied in thickness and the osteopenetrometer can adjust for this difference. Although we considered using a method that would test the entire cross sectional area of the proximal tibia at one time, it was determined that the varying thickness of the specimen, due to the resection angle, did not lend itself well to this method. The platens method used by Dong et al. was also considered,[43] but Keaveny et al.[42] demonstrated the susceptibility of this method to end effects which invalidate the continuum assumption and the data collected at the beginning and end of the experiment. Because Keaveny et al. achieved success using the end cap method; an attempt to replicate their method using lamb vertebrae was examined in a pilot study. However, the specimens were too thin and they broke in torsion (represented by a 45° angle crack in the cylinder) instead of compression. Upon further investigation using the ratio of diameter to thickness, it was determined that the specimens could not be tested using the end cap method. From the literature and pilot data, only the osteopenetrometer method developed by Sneppen[46] and improved by Hvid[44], [10], [45] seemed reasonable for testing the specimens in compression.

When the osteopenetrometer was first built in the 1980s, the software technology currently used was unavailable. Therefore, the machine was modified so that the bone resistance force would be transferred to the data acquisition program and could be graphed against the distance penetrated. The choice of needle diameters was validated by a study done by Hvid et al. in which they tested several needle configurations and found little to no difference between rounded needles and diameters varying from 3.3 mm to 2.5 mm with 90° cones and shafts milled down to 2.3 mm.[10] For this study, a 2.5 mm needle milled down to 2.3 mm with a 90° cone was chosen.

Trabecular Orientation

Beginning with Wolff's hypothesis in the mid 1800s, trabecular orientation has been associated with mechanical strength. Wolff's law can be summarized as: "every change in the function of a bone is followed by certain definite changes in internal architecture."[48] In relation to mechanical forces, Wolff's law suggests that a force placed on the bone will result in a change in architecture of the bone's structure. The reasoning for this adaptation comes from basic mechanics as shown when modeling the solution using the biological analog of minimizing stress on a simple cantilever beam. A force applied to the beam in pure compression will not cause a moment. However, a force at any other angle will result in a bending moment that will put unnecessary stress on the system. Therefore, to minimize stresses in the cancellous bone, any applied forces should be aligned parallel to the trabeculae. Recent studies have shown that, while Wolff's premise was correct, other factors including disease state,[38], [36], [39] variations in the bone shape,[15] and aging[37, 49] can affect the adaptation and structure of the bone in addition to the forces being applied.

The organization of the bone can be related to the degree of anisotropy of the material. Anisotropy represents a measure of the organization of the structures that comprises a material. This study used a method developed by Whitehouse in 1974[50] and expanded into a three-dimensional ellipsoid by Harrigan and Mann in the 1980s to determine the anisotropy of the bone.[51] The method used was called the mean intercept length (MIL), and it created a fabric ellipsoid using the eigenvectors and eigenvalues. An eigenvector (unit vector) represents a particular direction; in this study, the eigenvector models the direction of the trabeculae. The eigenvalues are scalar values that give the magnitude of the eigenvector, and in this study, the principle eigenvalue orients in the same direction as the majority of the trabeculae. Fabric describes the anisotropy of the bone with a fabric tensor being a positive definite second order tensor that mathematically describes the anisotropy by using the ratio of the eigenvalues and eigenvectors of the fabric tensor.[52], [53] A fabric ellipsoid can be created to represent the shape of the matrix.[51] An integral part in selecting the optimal resection angle comes from creating a fabric ellipsoid and determining the direction of the trabeculae, since trabeculae orientation can be related to mechanical strength and the ability to support tibial component fixation.

Null Hypotheses

By considering the importance of ligament balancing during total knee arthroplasty for varus patients, it appeared that purposefully cutting to 2° of varus, as done by Dr. Scott, improved tibial component instability and operation time. (personal communication) However, it was obviously necessary to determine mechanical stability and cancellous bone properties of the new resection angle in order to determine if this method truly was optimal or if it sacrificed cancellous bone strength to accommodate ligament balancing. This master's study was undertaken to address three questions. The null hypotheses for the study were as follows.

There will be no significant difference in compressive strength of the cancellous bone when comparing a varus and neutral resection of the proximal tibia.

The rationalize for this hypothesis was based on the research of Hofmann et al. that this was true in the anterior-posterior direction, resulting in a larger compressive strength[20] compared to the axis perpendicular resection technique (Figure 2). The same was assumed for the medial-lateral direction. The significance of evaluating a difference in angle in the direction came from Hofmann's study that examined the anterior-posterior direction but did not consider the medial-lateral direction.[20]

There will be no difference in regions of the proximal tibia specimen between the two resection angles.

Additionally, there was a need to consider the medial, lateral and central regions of the bone. Since Bloebaum et al. showed that strength varies based on region,[21] the study's null hypothesis was that there will be no significant difference in the compressive strength of regions of the proximal tibia in a varus patient during TKA when resected at a varus or neutral angle. The rationale for this hypothesis is that regional differences could exist, and it is important to see if they are different for the two resection angles because it is known that tibial component subsidence occurs primarily in the anterior-lateral region clinically.

Trabecular orientation will be aligned the same for both resection angles of the proximal tibia.

The orientation will be similarly aligned for varus and neutral specimens resected from a varus patient during TKA. Specifically, the degree of anisotropy (DA) will not be significantly different between the varus and neutral resection angle of the proximal tibia of a varus patient or between regions of the proximal tibia. The rationale for this hypothesis is that if there is no difference in compressive strength, which partially depends on the structure of the material, there should be no difference in trabecular alignment.[22]

METHODS AND MATERIALS

Study Design

The first criterion in the design of this study was whether to use animals, humans, cadaver tissue or patient tissue. Because of the difficulty in comparing proximal human tibia with animals, human tissue was chosen. Although most human studies use cadaveric tissue, the unique requirements of this study led to the decision to use patient specimens resected from patients of Dr. Scott, our study collaborator, undergoing a TKA. This decision required institutional review board (IRB) permission from both the Holy Family Hospital in Spokane, WA as well as the University of Utah/Veteran's Affairs Hospital in Salt Lake City, UT and both the WA IRB (#1361) as well as the UT organizations (#00023748) approved the study before it was conducted.

The next step was to collect specimens. The inclusion criterion for the study was that the patients must be undergoing a primary TKA. They also need to be at least 18 years of age, have a varus deformity of the tibia between 2-7° as measured using a goniometer on a long standing x-ray by Dr. Scott, have OA and have no other previous surgical procedures or diseases of the bone or cartilage for the knee being operated on. No personal identification information was sent to Bone and Joint Research Laboratory (BJRL). Originally, the study design called for 23 specimens per group, which was determined by doing a power analysis based on data from Hofmann et al.[20] who found that the axis-perpendicular method had an average compressive strength of 10 kN while the axis-parallel technique had a compressive strength of 15 kN. Inputting these numbers, along with a desire for 90% power, into Stata IC 10.0 (StataCorp LP, USA), a statistical analysis software program, showed that 23 specimens would be necessary for a similar study such as this one. Specimens were collected during surgery by Dr. Scott and were packaged in containers and shipped in dry ice and Styrofoam coolers overnight to the BJRL. Dr. Scott operated on the varus patients using his standard varus resection angle surgical technique. For the neutral specimens, Dr. Scott used a neutral cutting block on the patients and removed a slice of bone large enough to use for the study without compromising patient care before recutting the patient using his 2° varus cutting block. The result was that every patient ended up having the same surgery, a varus resection, with minimal added surgical time and risk.

Once each specimen arrived at the BJRL, it was cleaned off using a scalpel to remove remaining soft tissue other than marrow and cartilage. Care was taken not to damage the bone during this procedure. After being cleaned, the specimens were kept in a freezer at -20° C in a container until they were ready to be imaged.

Contact Radiographs

Before being mechanically tested, each specimen was radiographed. This was done by placing the specimen on one piece of CR5B developer paper (Agfa, USA) and loading it into the Faxitron Cabinet X-ray System (Faxitron X-Ray LLC, USA). The specimen was exposed for 25 seconds at 70 kV, although actual radiation appeared to go down to 67 kV during exposure. The specimen was radiographed with the resection side down as well as up. After exposure, it was developed using the CP 1000 (Agfa, USA) with corresponding G153 developer and G353 fixer (Agfa, USA). The contact radiographs were used to align the specimen correctly in the viewing window during Microcomputed tomography (MicroCT) analysis as well as to examine damage to the underlying structure that was not visible on the surface (Figure 5).

Microcomputed Tomography

In order to support hypothesis three, the bone specimens were imaged to examine trabecular orientation and degree of anisotropy. Although contact radiography shows the gross bone structure, using MicroCT for analysis allows for a better image of specimens.

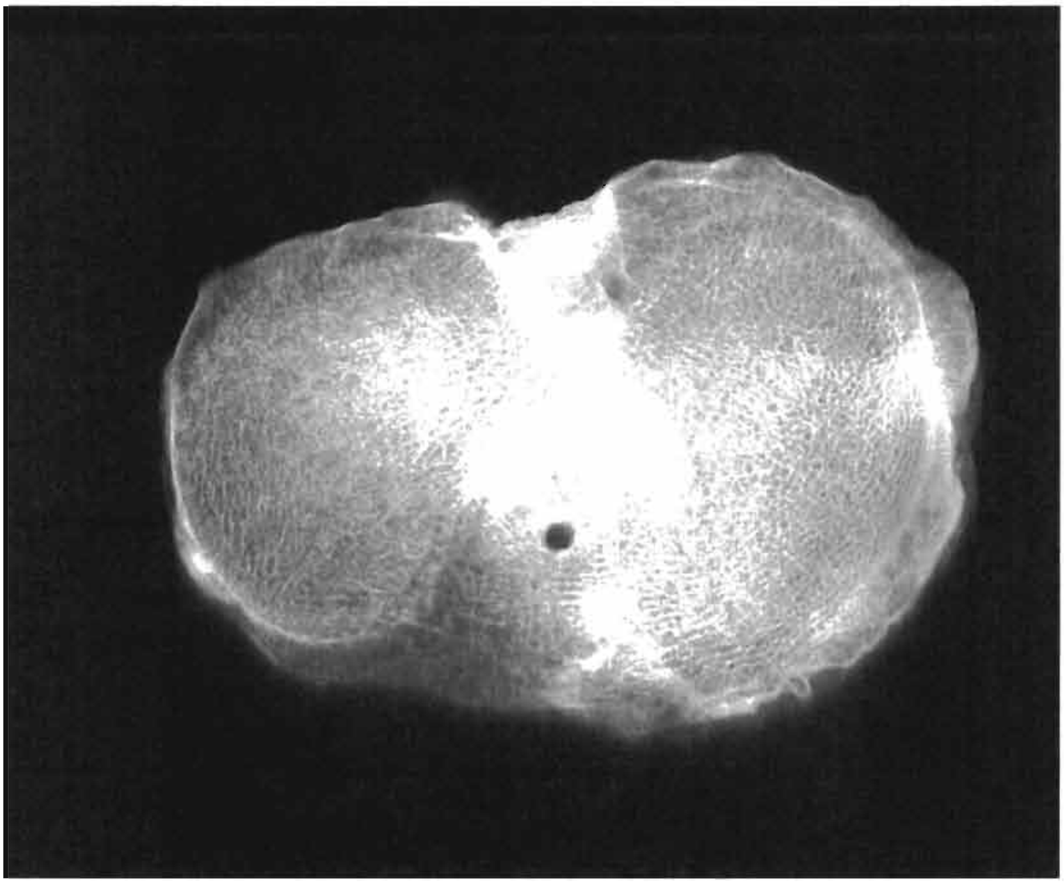

Figure 5. Radiograph of specimen 016. The holes visible are from surgery. The figure shows the structure of the bone and was useful for orienting images from MicroCT.

A MicroCT machine created a volumetric image of each specimen and reconstructed the image into a three-dimensional picture, which created a more sophisticated model of the trabecular structure than the radiographs. The MicroCT images were three-dimensional and allowed the cartilage and subchondral bone to be excluded during analysis. For optimal imaging, the specimens had to be sealed in a vacuumed container. The bags used were Seal-A-Meal Rivals and were cut to size so that the specimen fit inside with as little air space as possible. A volumetric conebeam Micro-CT system (eXplore RS, General Electric , USA) was used to image the specimens. The resolution was isotropic and the basic parameters were set to 46μm at 80 kVp and 450 μA. Because the equipment was volumetric, there was no slice thickness set and instead the machine created a three-dimensional image of every point in the specimen. This allowed any point in the bone to be selected and examined.

Each specimen had rubber bands lightly placed around the bag to minimize excess material so it could be placed on a flat holder and inserted into the machine. Two images had to be taken and stitched together since the size of each specimen was too much for one image collection cycle. The images were then reconstructed so that instead of 720 individual views, there was one three-dimensional complete specimen. The specimens were kept frozen until being placed into the MicroCT machine.

Once the datum for each specimen was compiled, it was analyzed first using SliceView software (SliceView 2.1 GE Medical Systems, USA) to reduce the file size to less than 800 MB which is the maximum allowable size for the analysis software. This was accomplished by dividing the specimen into two equal sections, using the region of interest tool, which had a scale of 0-1490 and as a result 745 was used as the midpoint.

Using this procedure allows for examining the region of interest without a possible loss of data due to too large of a file. After the file was reduced, both parts of the specimen were opened using MicroView software (MicroView 2.1 GE Medical Systems, USA) so they could be analyzed as a complete anatomical unit. The software allowed for selection of a region of interest (ROI) that could then be analyzed to determine the degree of anisotropy, eigenvalues, and eigenvectors. This information can be used to find trabecular orientation and compare the two different operative resection techniques. The region of interest was the same size, 4.6855 mm^3 every time but the position was determined by drawing a number (1-14) out of a box. The size of the region of interest selected allowed for the examination of a volume of bone to observe the complete regional area of bone that was affected during mechanical testing. However, care was taken not to sample the area in close in approximation to another mechanical testing site. This was done for a random hole (corresponding to the number chosen) in the lateral, central, and medial region of each specimen (Figure 6). The data were then compiled and analyzed. Degree of anisotropy data obtained from the bone analysis tool were organized into tables and then statistically analyzed using a Wilcoxon-Mann-Whitney test to determine significance between the varus and neutral resection angles for the whole specimens.

Mechanical Testing

The instrument selected for mechanical testing was developed by Sneppen and Hvid[44, 46] and allowed for testing small regions of cancellous bone in compression. The choice was made after researching other methods and selecting the one that most suited our needs. This process was detailed in the introduction section of this thesis.

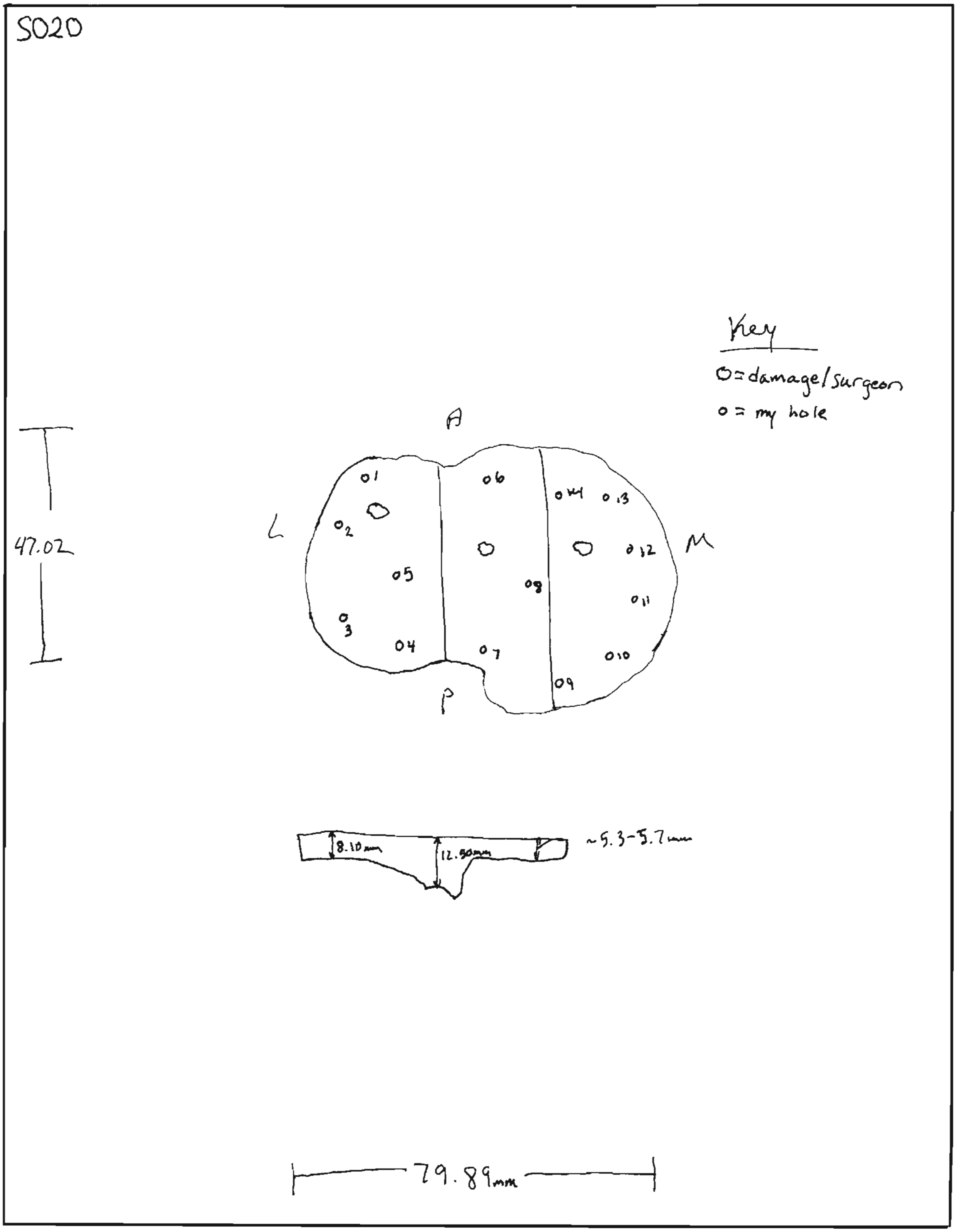

Figure 6. A representative map of specimen 020. Map was made according to the test protocol for mechanical testing at the orthopedic research laboratory. It was also used to orient the sample for MicroCT analysis.

Before a specimen could be tested, it had to be appropriately prepared. This necessitated cleaning each specimen a second time to be certain there was no soft tissue remaining (other than cartilage and marrow) that could influence mechanical properties. After that, the specimen was measured for thickness, length and width using digimatic calipers accurate to one-hundredth of a millimeter (Mitutoyo Corporation, Int.).

The average thickness in the medial region was 6.31 mm, lateral was 8.90 mm and central was 14.75 mm. The size of the specimen depended on the sex and age of the patient from whom it was obtained. The thickness of the medial region given (6.31 mm) was for testable areas only. All test areas were a minimum of 4.50 mm but in most cases were at least 5.30 mm. Only two specimens had some holes that were tested to a depth of 4.50 mm instead of 5.00 mm due to limited thickness of the specimens.

A map with the thickness and hole locations was created for the technicians to use during testing (Figure 6). Once the specimen was measured and areas too thin for testing were marked off using a black Sharpie® pen, 14 locations were drawn on the specimen according to position on the map. This number of sites represented the regions of the specimen while keeping the time needed for testing to a reasonable 30-60 minutes per specimen. The location for a hole was selected to avoid damaged areas from surgery, to avoid overlap with other holes and to completely remain in the trabecular region. The specimens were divided into lateral, central, and medial regions with approximately five hole locations in the lateral region, three in the central region and six in the medial region. Once this was completed, the specimens were returned to the freezer until approximately half an hour before testing. The specimens were thawed to room temperature, approximately 22°C as measured with a digital temperature sensor, and tested at that temperature.

In order to determine the best penetration speed, needle size and method of containing the specimen, pilot work was conducted. First, lamb vertebrae were used to determine approximate compressive strength of cancellous bone. The needle design to use for the osteopenetrometer was selected based on work done by Hvid et al. along with the rate to advance the needle.[54] The effect of distance advanced into the specimen on resultant force values was also measured (Figure 7). This was done by testing different thicknesses of lamb specimens to a depth of 3.00 mm as well as creating cylinders of the bone and attempting, unsuccessfully, to replicate the end-cap method used by Keaveny et al.[42] Instead of failing in compression, the cylinders failed in torsion at a 45° angle. Therefore the method had to be eliminated as a viable testing technique.

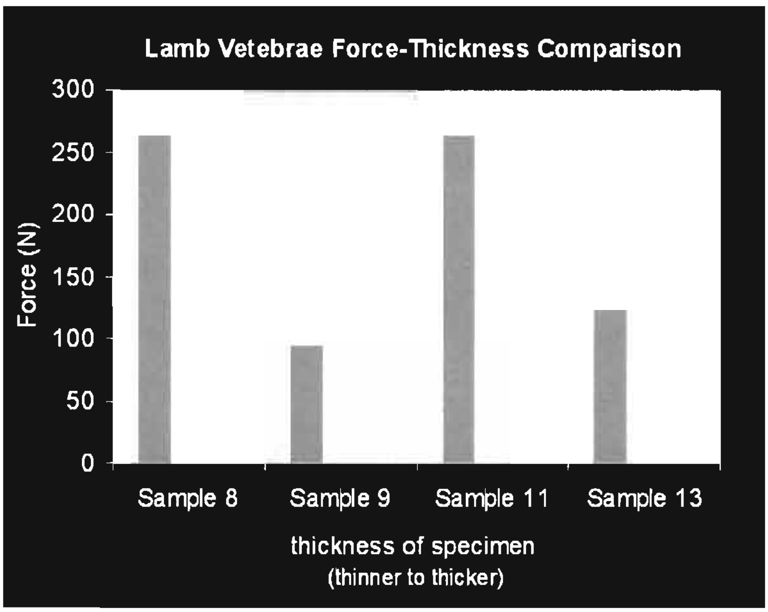

Figure 7. Graph of lamb bone forces. Four specimen of varying thickness were tested and showed no obvious trend in thickness that corresponded to force.

After testing with lamb bones, two human pilots were also tested. The pilot specimens helped refine the method of potting, placement of the holes, and estimated forces that would be detected for human proximal tibia cancellous bone. Refinement of the strain rate was especially important along with finding a method to stabilize the specimen during testing. A deformation rate of 0.05 mm/s and a depth of 5.00 mm were so that the corresponding strain rate was 0.025/s. This value falls within acceptable testing ranges for use with bone specimens with marrow as previously established by Carter and Hayes in 1977.[31]

Specimens were taken to the orthopedic research laboratory (ORL) for mechanical testing. Each specimen was embedded in Bondo™ (Bondo Corporation, Atlanta, Georgia) and sprayed with saline while the specimen equilibrated to room temperature. In order to be certain that there would be no damage to the specimen, and to make sure it would not be covered by the potting solution, the Bondo™ was mixed and poured into a pot first. Then, the specimen was lightly pressed down with resection side up and a level was placed on the resected surface to be certain that the placement would match that of the anatomical one (Figure 8). Enough Bondo™ was used that the specimen was encased on all sides except the resection surface and there was Bondo™ below to the extent that the specimen would never touch the bottom of the pot or the Instron. Once cooled, the Bondo™/specimen conglomerate was taken out of the pot to finish cooling. When it was back to room temperature, the specimen was ready to test.

As mentioned above, the choice of testing technique was a modified osteopenetrometer.[10, 44, 46] It utilized a surgical grade stainless steel needle 2.5 mm in diameter that was milled down to 2.3 mm with a 90° cone. The needle was attached to a

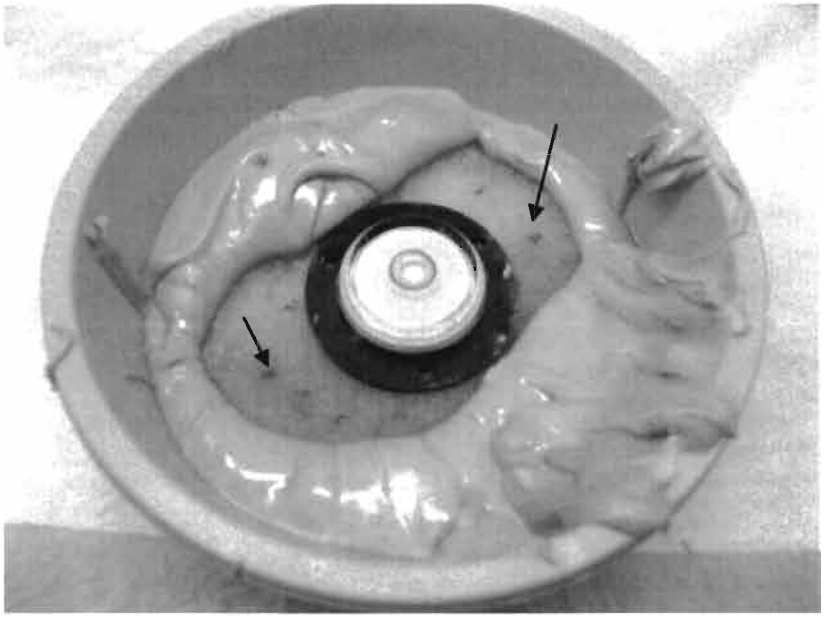

Figure 8. Preparation of specimen for mechanical testing. Specimen is placed in Bondo™ for stability. Hole locations are marked in black (see arrows) and the level shows it is properly aligned. The specimen was taken out of the pot before being tested.

load cell and inserted into an Instron. In this case, a model 1331 load frame with a model 8500 controller was used (Instron, USA). These were combined with a Sensotec load cell (Honeywell, USA) with a 1000 lb capacity and 0.2% accuracy. This was amplified by an Omega DMD-465WB strain amplifier (OMEGA ENGINEERING, Inc, USA) and read by a DAQPad-6030e A/D converter (National Instruments, USA). Data were collected using LabView 8.0 (National Instruments, USA) and a proprietary program written by one of the ORL technicians, Richard Vance.

The actual testing consisted of the needle being placed over each mark made based on the map created before testing (Figure 6), and systematically advanced into the bone, starting sequentially with mark one and ending with mark 14 (Figures 8 and 9). For each test, the needle compressed the bone at a rate of 0.05 mm/s for 4.5 or 5.0 mm (specimens 004 and 005 hole placements 10-14 only went down to 4.5 mm). The force-deflection curve for each hole (Figure 10) could be made from the data collected based on the proprietary software program written by Richard Vance. After testing, the specimen was placed back into the -20° C freezer. Ideally, this study would have been blinded, except the shape of the specimens left little or no doubt regarding the resection angle.

After collecting the forces and matching displacement values, the data were analyzed. In order to account for the varying thicknesses of the specimens, forces used for comparison were based on a percentage of the thickness. The rational for this comes from basic engineering principals, which relate force (F), stress (σ), depth (d), Young's modulus (E), strain (ε) and thickness (t) as seen in the equations below. Because thickness of a specimen is inversely proportional to the force and the depth is proportional, instead of comparing the force at a certain position, it is more accurate to compare forces based on percentages of thickness of each region of each specimen.

$$\sigma = E\varepsilon \quad (1)$$

$$\varepsilon = \Delta d/t \quad (2)$$

$$\sigma = F/A \quad (3)$$

$$F = AE\, \Delta d/t \quad (4)$$

Both 25% and 45% of the thickness of each specimen were chosen for the medial and lateral regions while only 25% could be used for the central regions. Therefore, 25% of the thickness of a sample in each region was calculated.

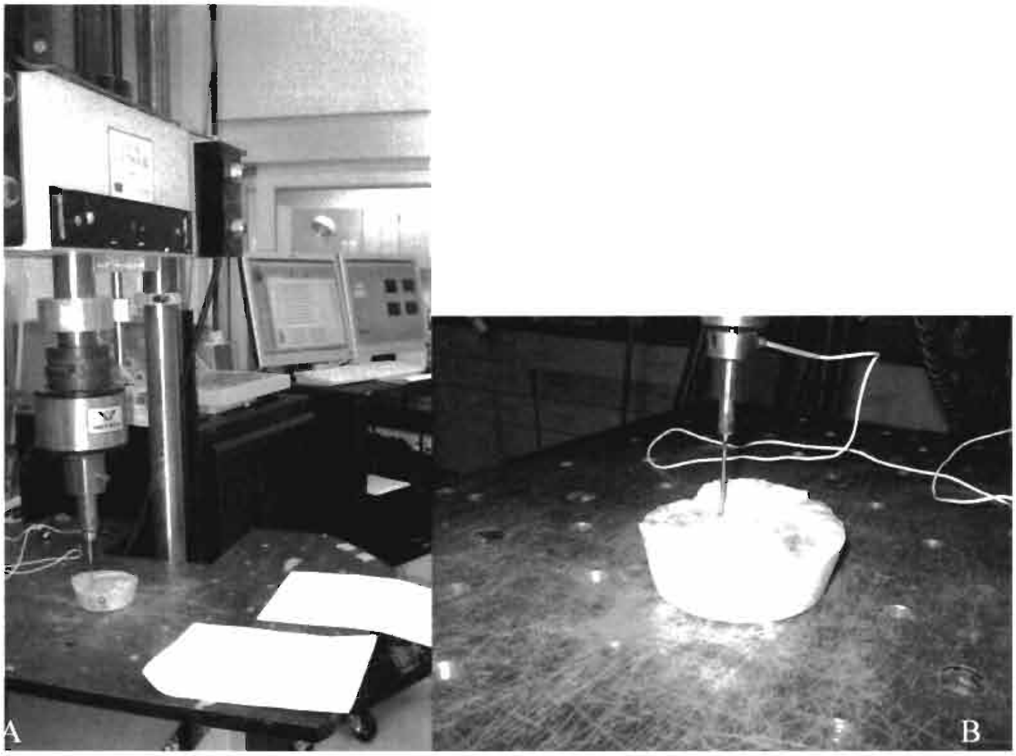

Figure 9. Osteopenetrometer set up. Image A shows computers used for data collection and the Instron and Image B depicts a close up of the needle set up on hole 1 of specimen 008.

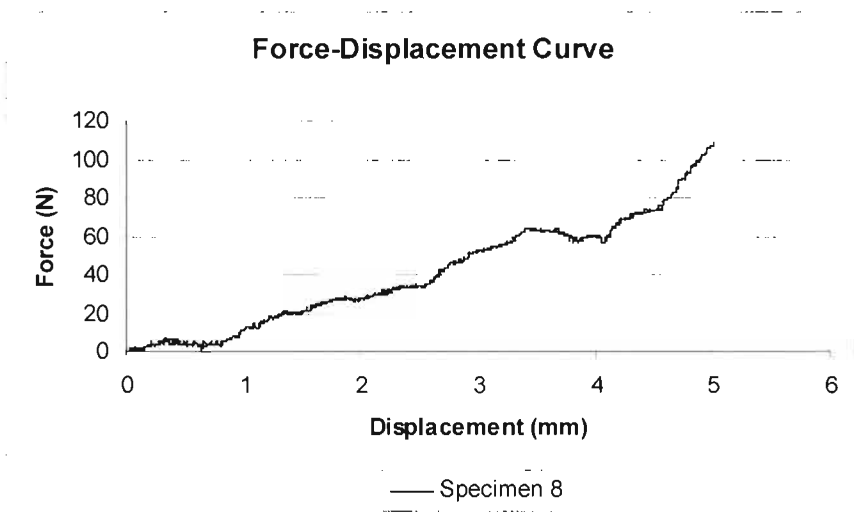

Figure 10. Representative force-deflection curve. Made from data obtained from Specimen 8.

This value was a depth and a matching force was chosen from the raw data file. The first force for that depth value was chosen to avoid biasing.

Once all forces were found for 25% and 45% of the depth for the regions, they were averaged together to obtain a mean force for the regions which would be used to answer hypothesis two. The means of each region were again averaged to obtain a mean for the varus and neutral specimens. This value was analyzed to answer hypothesis one. By comparing forces based on thickness instead of position, a more accurate representation of the compressive strength of the specimens was obtainable.

Imaging

In order to better understand how the mechanical testing affected the microstructure, two specimens were dried, embedded and examined in a scanning electron microscope (SEM). To examine resection angle microscopic differences, the second pilot specimen, a varus specimen, and the first real specimen, a neutral specimen, were selected. Because of the amount of time needed to prepare a specimen for SEM analysis, these specimens were chosen because of specimen availability and the process was not randomized. Additionally, one specimen, 011, a varus specimen, was radiographed after compressive mechanical testing. The image was used to see how the porosity of the structure affected the forces. Both these imaging techniques showed the effects of the needle penetration on the fragmented trabecular structure.

Scanning Electron Microscope

Before a specimen can be imaged with the SEM, the specimen has to have all water content removed and be embedded in polymethylmethacrylate (PMMA). Then, the embedded specimen must be ground down and carbon coated. The BJRL has a standard procedure for bone specimens, briefly described below.[55-57]

The specimen was first dehydrated in a Tissue-Tek VIP (Miles Laboratory, USA) for a 72 hour drying cycle while it was exposed to ethanol from 70% to 100%. This process removed the water from the specimen. It was then infiltrated with methylmethacrylate (MMA) in three steps over the process of 21 days. The specimen was placed into a plastic container before step one. For the first step the specimen was left in room temperature, but in steps two and three it was kept in a freezer at 4° C to prevent early polymerization. After completion of the third step, the specimen was placed under ultraviolet light and MMA solution was poured into it 2-3 cm at a time over a period of a week to allow for polymerization of the specimen. Once the specimen was completely embedded in PMMA, slices were made using a bandsaw in order to isolate the holes to be viewed (Rockwell Model 20, Rockwell International). After an appropriate section was cut out of each specimen, the slice was ground down using gritted paper (Leco) graded from 60-600 and polished using alpha alumina (1 μm, Leco). For the second pilot specimen, one hole was selected and for specimen 001, a slice with two visible holes was used.

After the specimen was polished, it was ready to be prepared and examined in the SEM using backscattered electron imaging (BSE). The first step was carbon coating it (Ted Pella, Inc, USA) and electrically grounding it on the viewing disc with copper tape (Ted Pella, Inc, USA). Specimen were individually examined using a JSM-6100 Scanning Electron Microscope (JEOL USA, Inc, Peabody, MA) in backscatter mode using a backscatter electron detector (Tetra, Oxford Instruments Ltd, Buckinghamshire, UK) and images were acquired with the Thermo Scientific software program (Thermo Fisher Scientific, Inc.). SEM settings were varied for different images with a constant voltage of 20 kV. The magnification changed from x12-x200 and the working distance varied from 12 – 36 mm as needed. Images were selected to observe holes made and to examine adjacent trabeculae but not to obtain measurements or conduct analysis.

Contact Radiograph

Specimen 011 was radiographed after being mechanically tested. This consisted of cutting and grinding away Bondo™ until the specimen was freed. There was minimal damage to the edges of the specimen but the interior was not changed. The specimen was again imaged for 25 s at 70 kV. All machines, paper and chemicals were the same as used for the previous contact radiograph images taken of all the specimens as mentioned above.

Statistical Analysis

The statistics for this study were determined using Stata as well as Microsoft Excel (Microsoft Int.). The graphs and tables were made using values from Stata® and Excel®. Preliminary determination of the alpha value was set at the beginning of the study based on the work of Hofmann et al. because they looked at a similar surgical method.[20] By lowering the alpha value from the standard 0.05 to 0.10, it was hoped that a significance that otherwise might not be there could be found. This was based on already knowing that clinically there were no failures and thus hoped to match that data with the statistical significance in this study. The degree of anisotropy means were analyzed using the Wilcoxon-Mann-Whitney test. For mechanical testing, the student t-test was used for the whole specimen comparisons and the Wilcoxon-Mann-Whitney test for the regional comparisons. The choice of tests depended on whether the standard deviation was more than one-third of the mean. If it was, the Wilcoxon-Mann-Whitney test was used to calculate p-values and if it was not, a student t-test was appropriate to use. Statistics were calculated with the help of assistant professor Greg Stoddard.

RESULTS

Sample Collection

Due to patient recruitment, surgeon availability and time constraints, the study concluded with n=10 for the mechanical testing and n=9 for the imaging. A later discussion explains the rational behind this discrepancy. All specimens were between 2-7° of varus. Specimens consisted of 15 males and 5 females whose ages ranged from 44 to 89 with an average age of 72.4 years. The patients had similar grades of OA and successful surgeries. Table 1 provides all of the deidentified patient data for each specimen with a complete data set and appropriate thickness that were received and tested.

Microcomputed Tomography and Trabecular Orientation

Once the region was selected (as described in the methods section), the bone analysis tool from MicroView created an ellipsoid with eigenvectors representing trabecular orientation with the largest one being the most prominent direction (Figures 11 and 12). In hypothesis three, the only interest was in seeing if the trabecular orientation complimented the mechanical testing results, and thus only the degree of anisotropy was statistically compared for neutral and varus wafers. The decision to compare trabecular orientation came from a similar comparison done by Bachus et al.[22] on the difference in resection angle in the A-P direction.[20]

Table 1. Deidentified demographic information on each specimen

Specimen Number	Age	Degree of Pre-operative Varus	Sex
1	84	5	M
2	84	2	F
3	66	5	M
4	50	2	F
5	73	4	M
6	67	7	M
7	N/A	N/A	N/A
8	82	4	M
9	72	6	M
10	88	4	M
11	67	5	M
12	N/A	N/A	N/A
13	N/A	N/A	N/A
14	89	7	M
15	87	5	M
16	71	5	M
17	74	3	F
18	44	4	F
19	N/A	N/A	N/A
20	61	4	M
21	63	4	F
22	N/A	N/A	N/A
23	82	3	F
24	N/A	N/A	N/A
25	N/A	N/A	N/A
26	77	6	M
27	66	3	M

The results demonstrated that there was no difference in the two resection angles in terms of degree of anisotropy (Table 2). A1, a2, a3 are the square roots of the corresponding eigenvalues. For assessment, degree of anisotropy for the lateral, central, and medial regions was given but was not statistically compared as the hypothesis only addressed the entire specimens for a varus and neutral resection angle (Table 3). The original purpose of the study was to determine if mechanical strength was compromised.

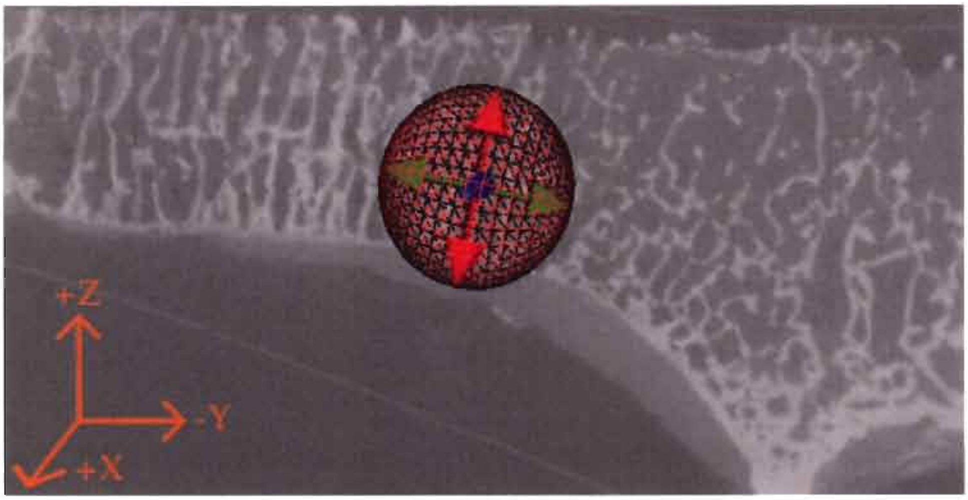

Figure 11. MicroCT ellipsoid of specimen 3 medial region. The fabric ellipsoid shows the direction of the trabeculae with the red vector approximately parallel to the primary trabeculae orientation.

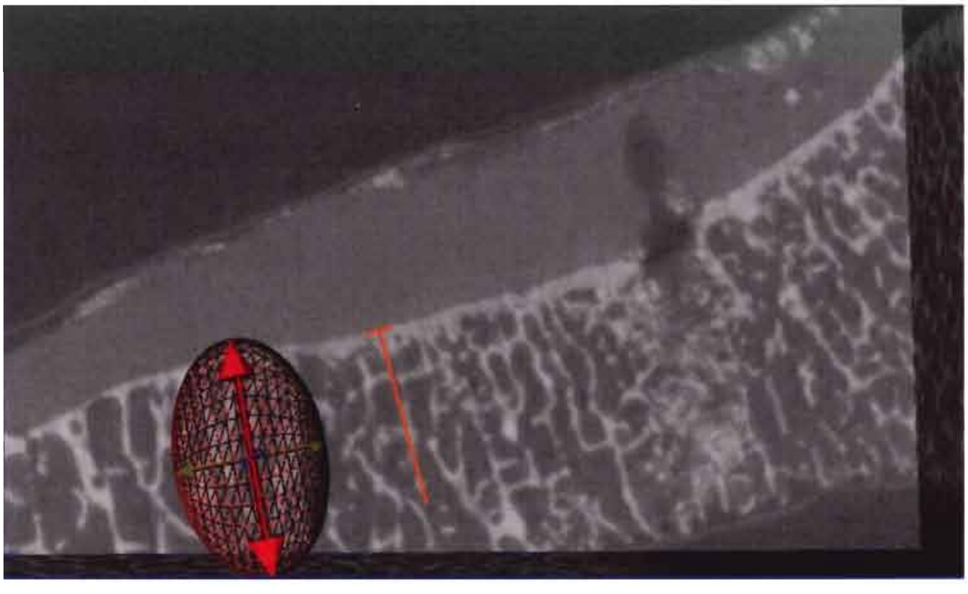

Figure 12. MicroCT ellipsoid of specimen 26 lateral region. The fabric ellipsoid shows the general direction of the trabeculae. The perpendicular line shows that the trabeculae are nearly all perpendicular to the articulating surface of the bone. The red vector represents the primary eigenvector which is approximately parallel with the trabecular orientation.

Table 2. Degree of anisotropy for whole specimen comparison of resection angle.

Degree of Anisotropy	Neutral[a]	Varus[a]	p-values[b]
	Mean (Range; SD)	Mean (Range; SD)	
a1/a3[c]	1.49 (1.13-2.15; .23)	1.42 (1.11-1.82; .19)	1.00
a2/a1[d]	0.83 (0.62-0.99)	0.81 (0.64-0.98)	0.96
a2/a3[e]	1.23 (1.06-1.73)	1.16 (1.01-1.61)	0.35

[a] This value is a ratio and thus has no units.

[b]The p-value of 1.00 is unusual and in this case suggests that there is no statistically discernible difference in the degree of anisotropy between the neutral and varus resection angles.

[c] This ratio is a measure of how anisotropic a material is. Fully isotropic is 1.00 and as the value increases, so does the anisotropy of the material.

[d] This ratio represents the degree of similarity between the primary and secondary fabric structures. Values closer to 1 correspond to a much stronger primary orientation.

[e] Another measure of relative anisotropy of the material in the local region.

Table 3. Degree of anisotropy for regions of the wafers.

Degree of Anisotropy[b]:	Neutral Lateral[a]	Neutral Central[a]	Neutral Medial[a]	Varus Lateral[a]	Varus Central[a]	Varus Medial[a]
	Mean (Range)	Mean (Range)	Mean (Range)	Mean (Range)	Mean (Range)	Mean (Range)
a1/a3	1.48 (1.22-1.85)	1.59 (1.19-2.15)	1.39 (1.13-1.66)	1.50 (1.28-1.82)	1.32 (1.11-1.65)	1.44 (1.16-1.68)
a2/a1	0.79 (0.62-0.88)	0.84 (0.75-0.96)	0.85 (0.67-0.99)	0.80 (0.68-0.98)	0.88 (0.78-0.98)	0.76 (0.64-0.97)
a2/a3	1.17 (1.08-1.27)	1.34 (1.06-1.73)	1.18 (1.06-1.27)	1.21 (1.03-1.61)	1.16 (1.01-1.30)	1.09 (1.03-1.15)

[a]No units since this is a ratio

[b] The ratios have the same definitions as in Table 2.

Hypotheses one and two addressed mechanical strength but also of interest was if bone alignment supported the mechanical testing results. Therefore, it was hypothesized that there would be no difference in trabecular orientation or degree of anisotropy between the whole wafers. Because Dr. Scott has reported no evidence of clinical failure (personal communication), there was no need to determine the structure of the bone in each region but this could be done in a future study.

Trabecular orientation correlates with the primary eigenvector as seen in Figures 11 and 12. The data showed that the neutral resection angle specimens have trabeculae more strongly oriented in the X direction (25 of the 27 tested sites) while the varus resection angle appeared to be primary in the X or Z directions (16 X and 9 Z). Table 4 represents three examples from each resection angle; the table listed the primary eigenvector and its corresponding eigenvalue.

To summarize, it was found that the degree of anisotropy does not vary between resection angles. This holds true for primary-tertiary eigenvector comparison as well as secondary-tertiary and secondary primary. When focusing on individual trabeculae, it appears that more are oriented in the Z-direction for a neutral resection angle. However, because individual trabeculae are not loaded and instead an entire region of the cancellous bone is loaded, the degree of anisotropy data collected and analyzed better answer hypothesis three. Therefore, the null hypothesis that there is no difference in resection angle was proven correct.

Table 4. Eigenvalues and Eigenvectors for determining Trabecular Orientation

	Primary Eigenvalue[a]	Primary Eigenvector[a]		Primary Eigenvalue[a]	Primary Eigenvector[a]
Neutral			**Varus**		
S001-L	27.49	[0.9934, 0.0886, -0.0733]	S005-L	13.1519	[0.9024, 0.0035, 0.4308]
S001-C	79.28	[0.8644, 0.1713, 0.4727]	S005-C	12.1603	[0.8048, -0.2721, 0.5276]
S001-M	22.05	[0.9664, 0.1120, 0.2314]	S005-M	3.1308	[0.8932, 0.0197, 0.4493]
S003-L	12.13	[0.9608, -0.0645, 0.2695]	S006-L	11.5911	[0.9839, -0.1787, -0.0055]
S003-C	30.51	[-0.9548, 0.1483, -0.2575]	S006-C	12.2201	[-0.7546, -0.0053, -0.6562]
S003-M	20.00	[0.9973, 0.0430, -0.0592]	S006-M	4.7261	[0.6755, -0.1456, 0.7228]
S004-L	14.09	[0.7703, 0.3321, 0.5443]	S008-L	12.7561	[0.6763, -0.1838, -0.7133]
S004-C	16.22	[0.8393, 0.2554, -0.4799]	S008-C	14.2545	[0.8059, 0.0511, -0.5899]
S004-M	8.73	[0.9877, -0.0450, 0.1500]	S008-M	10.4334	[0.5156, -0.0349, 0.8561]
S009-L	18.60	[0.9146, 0.1139, 0.3879]	S011-L	21.6863	[0.9371, 0.0460, -0.3459]
S009-C	12.46	[0.1876, -0.3958, -0.8990]	S011-C	16.7943	[-0.4744, -0.1572, -0.8662]
S009-M	17.91	[0.8561, 0.0739, -0.5115]	S011-M	4.5679	[-0.0143, 0.1255, 0.9920]
S0010-L	16.00	[0.9769, 0.1712, 0.1279]	S014-L	19.6194	[0.7771, 0.1305, 0.6157]
S0010-C	11.78	[-0.9503, -0.2902, -0.1126]	S014-C	21.902	[-0.4750, -0.0867, -0.8757]
S0010-M	10.13	[0.9669, -0.0030, -0.2550]	S014-M	3.7602	[-0.4867, -0.7003, -0.5223]
S0015-L	4.85	[0.9839, -0.0078, 0.1783]	S016-L	9.6353	[0.8290, -0.1816, 0.5289]
S0015-C	9.57	[0.6572, 0.5998, 0.4565]	S016-C	12.5727	[-0.9247, -0.2234, 0.3083]
S0015-M	15.28	[0.8570, -0.0809, -0.5089]	S016-M	10.5541	[-0.9192, -0.1072, -0.3789]
S020-L	14.21	[0.9675, -0.1863, 0.1707]	S018-L	9.3902	[0.5209, 0.0235, 0.8533]
S020-C	5.73	[0.8868, -0.1388, 0.4408]	S018-C	17.6544	[-0.8074, 0.2693, -0.5250]
S020-M	11.89	[0.8917, -0.1275, 0.4342]	S018-M	11.9922	[0.9771, -0.0560, 0.2051]
S026-L	19.23	[0.9495, -0.1289, -0.2860]	S021-L	27.0121	[0.9204, 0.3804, 0.0901]
S026-C	15.38	[0.9850, 0.1384, -0.1026]	S021-C	19.6643	[0.9645, -0.0749, 0.2532]
S026-M	8.78	[0.9751, -0.0635, -0.2126]	S021-M	7.4264	[0.5337, 0.0187, 0.8455]
S027-L	17.63	[0.9956, -0.0512, 0.0785]	S023-L	12.9503	[0.7265, 0.1672, 0.6665]
S027-C	20.75	[-0.8655, 0.4758, -0.1568]	S023-C	1.4787	[-0.2541, 0.9666, 0.0339]
S027-M	1.13	[0.6509, 0.1206, -0.7495]	S023-M	9.6791	[0.8237, -0.5396, -0.1744]

[a] There are no units for the eigenvalues or vectors

Mechanical Testing

During pilot testing, the data showed that force and distance were inversely related. Additional testing on different thicknesses of the lamb bones showed forces were not entirely dependent on thickness. However, because force is related to thickness, this relationship was taken into account during data analysis.

The osteopenetrometer method used for mechanical testing centered on a small area of cancellous bone in order to measure changes in regions. By collapsing the data into means and analyzing, a comparison of the differences in the whole specimen resection angle was also determined. It was important to note that forces were highest in the medial region, which supports the results of Bloebaum et al..[21] The weakest area was the central region, which complements the biomechanical function as there is little to no load placed directly on the central region of the tibial plateau. The data showed the lateral region had forces that were higher than the central region but still lower than the medial region. The varus resection angle (medial region of specimen 16) exhibited the greatest force seen of 760 N but there was no statistical difference between the neutral and varus medial regions.

The depth value chosen for comparison was based on either 25% or 45% of the thickness of the specimen at the location of each hole and thus the value varied for each specimen, each region and sometimes between holes in a region. Only the first force value for each corresponding depth value was selected to statistically compare to help avoid biasing. This resulted in nine values being selected for each of the fourteen holes made in a wafer. The data were then reduced into means in order to avoid the fact that each datum point was not independent of the other. The means for the regions were again averaged to obtain one value for all the varus and one value for all the neutral specimens.

No difference in the regions or the whole specimen between resection angles was found (Figures 13-16). This was with an alpha level of 0.10, which was originally chosen in order to have a wider range of significance as it was thought that varus would be stronger than neutral but only slightly. However, even using the more stringent criterion

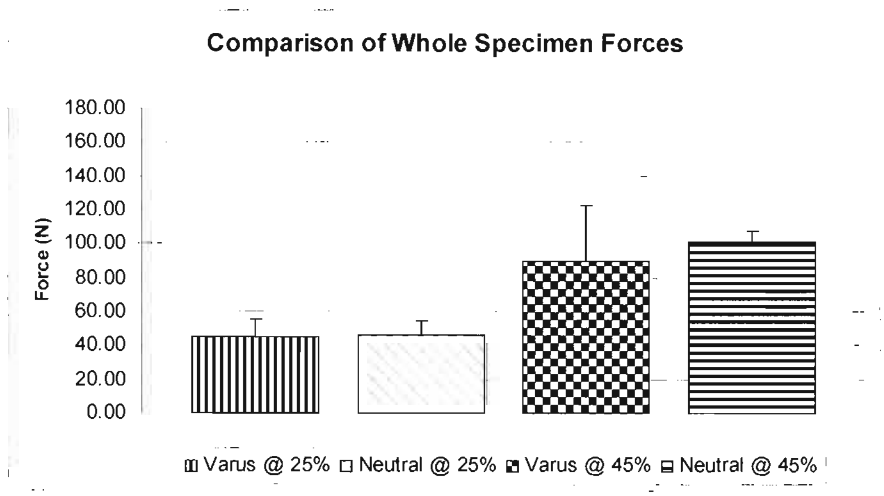

Figure 13. Comparison of mean force values between neutral and varus resection angles. The forces were calculated by computing the mean of each hole and averaging those for each resection angle. The mean of the varus was 44.73 ±10.45 N at 25% and 90.41 ±32.18 N at 45%. The mean force for the neutral was 46.05 ±8.47 N at 25% and 101.72 ±6.25 N at 45%. The p-value was 0.87 for 25% of the thickness and 0.71 for 45%. No difference was observed between the two resection angles.

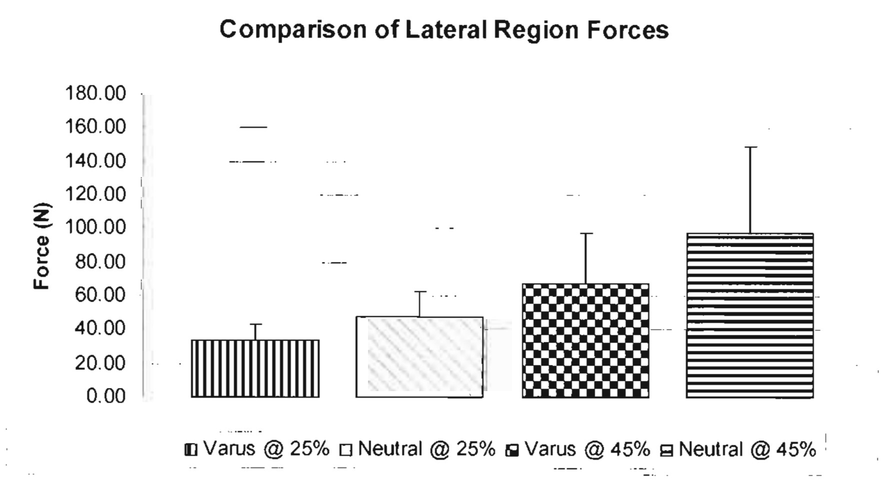

Figure 14. Comparison of mean lateral force values between resection angles. Holes in the lateral region were averaged and the mean for each resection angle determined. The mean of the varus was 33.48 ±14.53 N at 25% and 67.66 ±30.06 N at 45%. The mean for the neutral was 47.51 ±23.83 N at 25% and 97.29 ±51.35 N at 45%. The p-value was 0.16 for 25% of the thickness and 0.16 for 45%. No difference was observed in the lateral region.

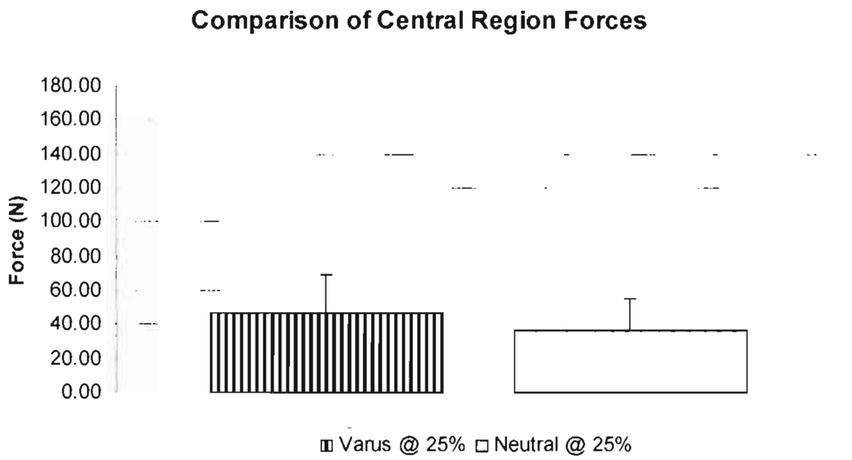

Figure 15. Comparison of mean central force values between resection angles. Holes in the central region were averaged and the mean for each resection angle determined. The mean of the varus was 46.57 ±22.34 N and the neutral was 36.94 ±18.42 N. The p-value was 0.34 for 25% of the thickness. Due to the thickness in the central region, 45% could not be analyzed. No difference was observed between the central regions.

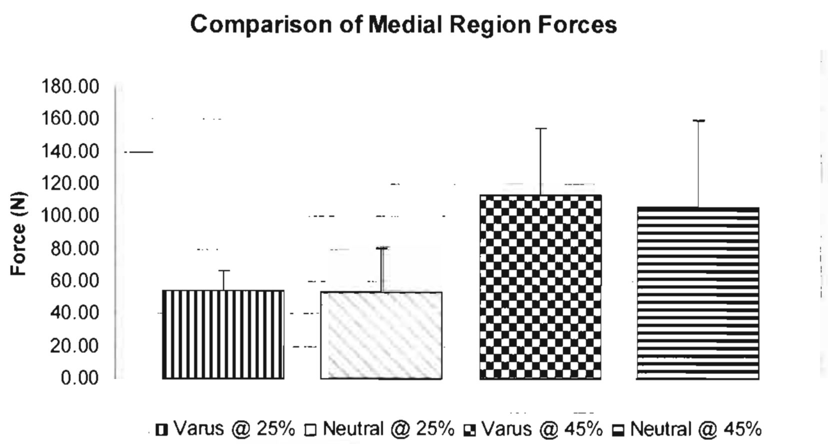

Figure 16. Comparison of mean medial force values between resection angles. Forces in the medial region were averaged and the mean for each resection angle determined. The mean of the varus was 54.14 ±12.26 N at 25% and 113.17 ±41.55 N at 45%. The mean for the neutral was 53.69 ±26.96 N at 25% and 106.14 ±53.71 N at 45%. The p-value was 0.73 for 25% of the thickness and 0.62 for 45%. No difference in forces was observed in the medial region.

of 0.05, there is still no difference between resection angles ($p=0.87$, 0.71, 0.16, 0.16, 0.34, 0.73, 0.62).

The mechanical testing data supported what was found using the MicroCT as well as what has been observed clinically. Although not significant, the lateral region forces were slightly higher for the neutral resection angle ($p = 0.16$ and 0.16) and the medial region forces were slightly higher in a varus resection angle ($p = 0.73$ and 0.62). This difference could be due to remodeling of the bone as a varus patient will preferentially load the medial side more than the lateral side.

Imaging

To determine that the osteopenetrometer setup performed as predicted, SEM images of two specimens were collected and examined. The images clearly showed the penetration of the needle stopped at exactly the depth specified. Observations showed no disturbance of adjacent trabeculae (Figure 17) and therefore lead to a conclusion that the effects of the mechanical testing were regional as intended.

A contact radiograph of specimen 011 was taken to show the damage done by the holes as well as to determine that the needle had gone in straight (Figure 18). Some holes show darker than others which could be due to porosity or a higher force. All fourteen holes can be seen and show that the penetration of the needle was circular and did not deviate from its path as confirmed on SEM analysis.

Statistical Analysis

In order to compare the resection angles, data was collected with both mechanical testing and MicroCT. Before the study began, assistant professor Greg Stoddard assisted

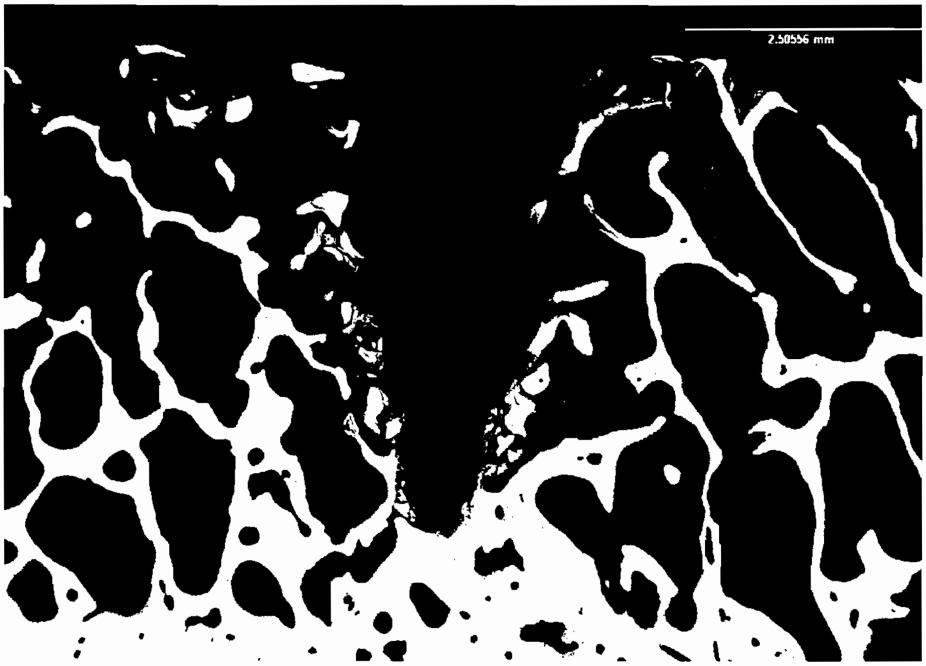

Figure 17. SEM of specimen 001 after mechanical testing to show pin penetration. The image was taken at a working distance of 36 and magnification of x12. Only regional damage to the trabeculae could be seen in the image.

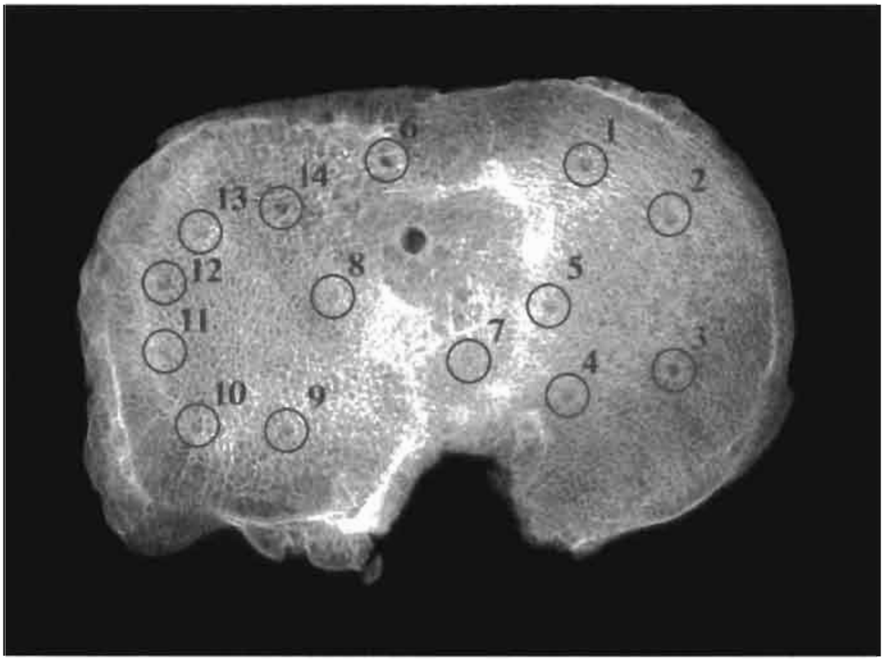

Figure 18. Contact radiograph of specimen 11 after mechanical testing. This figure showed the 14 holes made by the osteopenetrometer on specimen 011. The holes that were not circled were made by a surgeon or were damage to the specimen in vivo or during surgery. The contact radiograph was made with a time of 25 s and radiation of 70 kV, which went down to 67 kV during actual radiation.

in calculating the sample size needed to achieve 90% power with an alpha value of 0.10. Values were taken from Hofmann et al.,[20, 22] and a required sample size of 46 total (n=23 per resection angle) was determined. However, the amount of time it took to obtain IRB approval in two states as well as the amount of time to collect samples meant only 20 specimens could be collected before the study had to be closed to enrollment in order to complete the analysis in a timely manner.

Because the specimens were not the same thickness, the variability was accounted for by analyzing forces obtained from 25% and 45% of the thickness of each region of each specimen as previously explained. A mean for each region was taken and averaged to obtain a mean value for the varus and neutral resection angles. In some instances, the data could be analyzed with a student t-test but sometimes the standard deviation was more than one-third of the mean and in that case the data were then analyzed with the Wilcoxon-Mann-Whitney test and the derived p-values were reported.

A difference in resection angles was not found, either in the whole specimens or in the regions during mechanical testing. Degree of anisotropy measurements also did not show significance between neutral and varus. Therefore, the study has determined that there was no significant difference in compressive strength or trabecular orientation between the neutral and varus resection angles for varus patients undergoing a primary TKA when the angle being compared is 2° of varus against 0° (neutral).

DISCUSSION

Hypotheses

The first and second null hypotheses were related by their dependence on mechanical testing. The first null hypothesis was supported. Therefore it can be stated that there was no difference between the varus and neutral resection angle. The second null hypothesis divided the specimens into regions. Once again, no difference was found between regions of the bone when comparing forces as a function of the thickness of each specimen.

The third hypothesis and its subcomponents relate to trabecular orientation and degree of anisotropy. Although originally meant to be simply observed and not analyzed, the degree of anisotropy was statistically compared between specimens and found to be non-significant ($p=1.00$). Relative degree of anisotropy and relation to primary orientation also showed non-significance ($p=0.35$, $p=0.96$). Because of the high p-values and since this was not part of the original study design, the trabecular orientations in the regions of the specimens were not statistically compared. Another study could compare the regional trabecular orientations to determine if there was a difference. Mechanical testing suggested that no difference would be found.

Although degree of anisotropy was highly correlated with trabecular orientation, Table 3 was provided to illustrate the primary directions of the trabeculae in terms of eigenvalues and eigenvectors of representative specimen. The neutral resection angle has more trabeculae oriented in the X-direction. However, since individual trabeculae are usually not as important as a region, this possible difference does not affect the results which show that there was no difference in the two resection angles when a region is compared. Using the information from comparing degree of anisotropy, it can be concluded that the null hypothesis which stated there would be no difference in degree of anisotropy and trabecular orientation between resection angles can be accepted.

Mechanical Testing

The author is confident that the testing method yielded accurate results, which allowed for correct comparison between resection angles. By assuming the bone was a continuum in the regions tested, the study values could be compared to those in the literature. In order to appropriately compare, a strain rate of 0.025/s and an area estimation of $4.9*10^{-6}$ allowed a conversion of the force-displacement values into ultimate stress-strain values.[31, 58] Values for this study's cancellous bone ultimate compressive strength ranged from 6.9 MPa in the neutral-central region to 26.4 MPa in the neutral-medial region and 7.5 MPa in the varus-central region to 28.1 MPa in the varus-medial region. These values agree with the literature which estimates trabecular bone to vary between 3.5 MPa[31] to 41.0 MPa.[58] The medial region was higher than the other two regions, but the values were lower than those reported by Hvid et al. perhaps because this study's bones were from OA knee patients.[58] The graph shape and force measured in this study was similar to that determined by Sneppen et al. and Hvid et al. (Figure 19).[10, 44, 46] Initial differences between the values in the literature and this study arise because of the source of the specimens. Sneppen et al. and Hvid et al. used

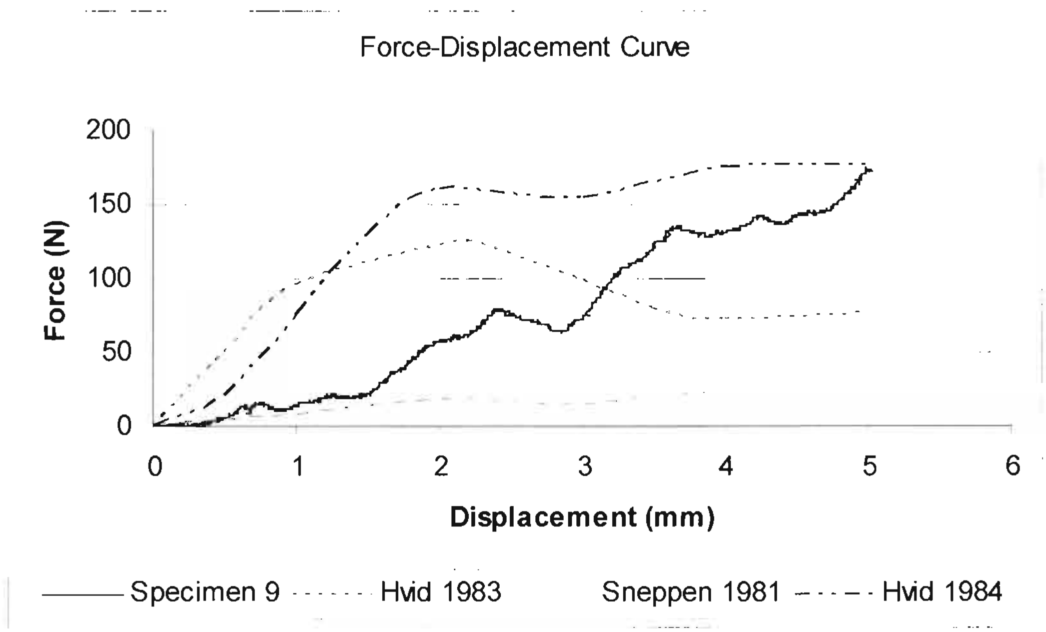

Figure 19. Curve comparing study data to literature. Data from the current study compared with other curves made from data collected by Sneppen et al. and Hvid et al. which shows similarities between studies.[10, 44, 46]

proximal tibia human bone but they removed all cartilage and sliced the specimens so they would have a uniform thickness.[10, 44, 46] Because this could not be done, this study's force values will be slightly different. However, the curve shape showed similarity and values are in a similar range.

The method showed good comparison to the literature. Therefore, these results, which showed that there was no difference in the individual regions (lateral, central, and medial) as well as between the entire specimens, can be accepted as scientifically valid results obtained in a comparable manner to previous studies.[10, 31, 44, 46, 58]

Microcomputed Tomography

The purpose of doing the MicroCT analysis on the specimen was to examine trabecular orientation and degree of anisotropy. The relationship between trabecular orientation and strength comes from Wolff's hypothesis. In this study, there was no significant difference in resection angle even though the bone was varied in size. The traditional interpretation of Wolff's law suggested a difference in force between the resection angles.[48] Thus other factors besides Wolff's hypothesis, such as the small degree of angle change and anatomical alignment of the proximal tibia from the disease state, have a stronger impact on the compressive strength of the bone as demonstrated by Hofmann et al.[20]

Anisotropy of a material can be related to trabecular orientation. The primary direction, found in measurements for the anisotropy of a material, directly correspond to the orientation of the trabeculae for that region. In the current study it was possible to see this correlation (Figures 11 and 12) when comparing the fabric ellipsoid with the orientation of the trabeculae. Therefore this study showed that the primary directions of the trabeculae are oriented with the surface that was tested mechanically. However, because no statistical difference in compressive strength or degree of anisotropy was found in resection angle, Wolff's hypothesis was not as prevalent in this situation. A larger difference in angle may change the relevancy of Wolff's hypothesis.

The decision to study trabecular orientation was made based on a study done by Bachus et al.[22] as a follow up to the study done by Hofmann et al. that compared resection angles in an anterior-posterior direction.[20] In the Bachus et al. study, the data showed that the trabeculae were oriented nearly vertical with the anterior-posterior parallel resection technique but not with the axis-perpendicular technique. The angle of the trabeculae corresponded with an ability of the resected proximal tibia to withstand a higher load for the parallel resection technique. For hypothesis three, it was found that there was no significant difference in the degree of anisotropy between the two resection angles and no difference in cancellous bone compressive strength. The difference in results between the current study and the study by Bachus et al. could be contributed to the small degree of varus (0°-2°) used in this study compared to a higher difference in posterior slope degree (8.5°-12.0°).[20, 22]

Clinical Significance

Most surgeons attempt to fix mild to moderate varus deformities of the proximal tibia during TKA by cutting the proximal tibia to a neutral alignment before placement of the tibia TKA components. They then usually have to balance or release the MCL since this realignment of the proximal tibia results in a tight MCL. Dr. David Scott uses a customized 2° varus cutting block from Stryker© to keep the patients in some degree of varus. (personal communication) He employs this technique on both cemented and uncemented TKA and learned the method during his fellowship with Dr. Hofmann. It is utilized on patients with a need for a primary TKA and a varus proximal tibia. Dr. Scott selects patients using a goniometer and has chosen to do this method to reduce or even eliminate the need to perform ligament balancing.

Because Dr. Scott keeps the patient in varus, he does not ignore the patient's physiology and consequently has little to no need for ligament balancing. This reduces time in the operating room, maintains stability of the knee and lowers the added risk to the patient when operation time is extended. Properly balanced ligaments reduce excessive wear, osteolysis and prevent early revision. Although Dr. Scott has not had to revise his TKA patients in his 11 years of using the 2° varus resection angle, he had no mechanical or imaging justification for using the varus resection method until this study was performed.

This study was undertaken to compare proximal tibia bone strength between the neutral resection angle used in current operative techniques with a 2° varus resection angle. The study results support the clinical observations of Dr. Scott in that there has been no tibial component subsidence to date, tibial component fixation has been maintained, and ligament balancing requirements have been avoided. (personal communication) To these observations, it can be add that the load carrying ability of the proximal tibia was not compromised using the technique.

Limitations of the Study

Although the results of the study were promising, there are several limitations that need to be addressed. First was the limited sample size. Even though the study used previous literature to determine sample size, the number of samples calculated as needed for 90% power was not feasible in the time required to finish the study. Therefore, instead of using 23 specimens per group as calculated at the beginning of the study, the study concluded with 10 specimens in each group. Additionally, due to corrupted data and researcher error, one specimen from each group had to be removed for MicroCT analysis, which left 9 per group.

The use of only one surgeon avoided interoperative error. Dr. Scott is very familiar with the technique, but taking samples from only his patients limits the patient population for the study. Because Dr. Scott uses a 2° cutting block, regardless of patients' original degree of varus deformity, he is potentially limiting the conclusion since patients originally had deformities from 2-7°, which could affect the structure of the bone. However, because a difference in resection angle was not found, it was probably valid to suggest that the angle of cut was compared to original varus deformity was not significant in this study population.

The third limitation of the study comes from the design for mechanical testing. Although very preliminary pilot testing included examining different thicknesses of lamb vertebral cancellous bone and found no noticeable difference, the thickness of the human samples in a composite could have an effect on the results. Composite theory shows that thicknesses of each material in the composite when stacked together can change the mechanical properties.

The mechanical testing data were analyzed to include the effects of thickness by selecting forces based on percentages of the thickness within each of the three regions of both. However, the thickness of the specimen was not an easy factor to control since the specimens were taken from human patients and bone quality and thickness remaining could not be compromised. Therefore, a uniform thickness for every specimen was unattainable, as would be ideal for comparison. In order to account for this, the force values obtained from mechanical testing were analyzed as a function of the thickness.

Summary

This master's project was designed to compare resection angles in the medial/lateral direction on a primary varus TKA patient. The purpose was to determine if compressive strength of the cancellous bone in the proximal tibia was compromised by cutting the proximal tibia at a varus angle compared to the traditional neutral angle. The study received IRB approval to use tissue from patients undergoing primary TKA at the Holy Health Family Hospital in Spokane, WA. Knowledge of the literature in regards to mechanical testing of cancellous bone, examination of trabecular orientation and surgical methods used on TKA patients was imperative. Three null hypotheses were proposed and examined.

The first two null hypotheses compared compressive strength of the specimens from two resection angles for 14 holes representing the whole specimen as well as three regions within the specimen. A third hypothesis correlated the trabecular orientation and degree of anisotropy to the compressive strength. In all instances the null hypotheses were accepted. Therefore this data helps justify using the 2° varus resection technique on a varus patient. With no significant difference in compressive strength, the varus technique does not appear to compromise mechanical stability, while helping to reduce a need for ligament balancing. The degree of anisotropy between the two resection angles is also not significantly different. The data from this study supported that a varus resection angle for a patient with a varus proximal tibia receiving a primary TKA can be clinically efficacious and safe.

Future Studies

Using the data collected in this study, a sample size of over 600 would be needed to show 80% power for the medial region. This might be possible to collect by conducting a multicenter study involving several surgeons. This large difference in sample size from that first calculated for this study can be explained for a few reasons. First, power analysis only provided a guideline to obtain potential sample size. Second, literature data from only one study that had a similar study design was used; however, it examined a different angle and only healthy patients. Therefore, it was not a perfect predictor of the power required for this investigation. Finally, clinically there has been no evidence of failure with over 1500 varus resection angle surgeries performed which again suggests a large number may be needed to find significance with a power of 80% or more.

Studies could also examine the effects of specimen thickness on compressive strength data by using human cadaver tissue that could be cut to the same thickness and examined. The tissue would not necessarily be OA or have a varus degree, but it would allow a research to determine if a uniform thickness of the specimens will affect the compressive strength compared to analyzing the forces as a function of thickness with varying thicknesses of specimens.

Another study could examine specimens for ash content, bone volume fraction and other measurements of bone that help complete the analysis of the resected tibia. Along those same lines, future research could also test whether other methods for finding the fabric tensor besides MIL would give different results. All of these studies would provide stronger support to the findings that there is no difference in mechanical stability of the tibia component of a varus patient when resecting at a varus angle compared to a neutral angle during a primary TKA.

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